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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/305,084	05/04/1999	Robert J. Schneider	5914-080-999	1583

20583 7590 03/27/2008

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
03/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/305,084	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2008 has been entered.

Claims 43 and 45 have been amended. Claims 43-59 are pending and under consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient having melanoma by the selective antagonization of the ETB receptor comprising the administration of known peptide antagonists of ET(B) receptor and antibodies which antagonize the ET(B) receptor, does not reasonably provide enablement for a method of treating a patient having melanoma by selectively antagonizing the ET(B) receptor by means involving the administration of nucleic acids targeting the expression of endothelin B, such as ribozymes and triple helix formation, or a method for preventing the development of a melanocyte to primary melanoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A) As drawn to the treatment of cancers by administration of nucleic acids for the degradation of an mRNA product in vivo

The specification states on page 26, line 23 to page 27, line 2, that gene therapy approaches including ribozymes and triple helix molecules are contemplated as part of the invention as inhibitors of the activation of ETB and the progression to melanoma. James and

Gibson (Blood, 1998, Vol. 91, pp. 371-382) teach that many of the problems associated with the use of ribozymes are similar to those of antisense oligonucleotides, such as attaining efficient cellular entry, ribozyme stability in vivo and precise targeting to the desired RNA sequences which are complicated by the existence of RNA-ribonucleoprotein complexes, and the availability of divalent cations in the cellular milieu (page 374, second column, lines 16-30). James and Gibson teach that the efficiency of the ribozyme is also dictated by the sequence context of the target site which can alter the rate of cleavage by more than 100-fold difference (page 377, second column, lines 20-30). James and Gibson also teach that the accessibility of the target site must be assessed either empirically or by computer modeling which is less expensive, but provides less reliability than empirical methods. One of skill in the art would reasonable conclude that the same technical issues as applied to in vivo stability and targeting would also exist for the formation of a triplex DNA in vivo.

The specification does not remedy any of the deficiencies or the prior art with regard to the administration of a nucleic acid targeting the expression of the endothelin B receptor. Given the lack of any guidance from the specification on any of the above issues pointed out by James and Gibson. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the methods of claim 26 to the extent that it reads on gene therapy.

(B) As drawn to the preventing the development of a melanocyte into melanoma in a patient.

The instant claims are drawn in part to a method of preventing the development of primary melanoma from a melanocyte comprising administering to a patient in need thereof a compound that is an endothelin B receptor specific antagonist. When given the broadest reasonable interpretation, the claim encompasses the prevention of melanoma in a patient who has never had melanoma. The art teaches that the initiation of cancer is a mutational event (the abstract of Ramel et al, Environmental Science Research, 1984, Vol. 41, pp. 97-112, cited in a previous Office action). The specification teaches that ETB receptor antagonists inhibit the early events associated with melanoma development. However, the specification does not teach how to use the instant methods to inhibit the initiation of melanoma, because there is no nexus between the administration of the ETB antagonists and the prevention or reversal of a mutational event such that the primary initiation event in melanoma is prevented. Further, the specification

does not teach how to identify a "patient in need thereof" wherein said patient is treated with the ETB antagonists before the mutational event that leads to initiation of melanoma, because said patients would be without atypical lesions because initiation, by definition, precedes progression.

All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicants amendments.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643